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Commentary

Lung biopsy in ARDS: is it worth the risk?

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Abstract

Progress in the treatment of acute respiratory distress syndrome (ARDS) has been slow, perhaps in part due to the heterogeneity in the biology underlying this syndrome. Open lung biopsy is a feasible approach to define various subcategories of underlying histology. In experienced hands, with careful selection of patients and close attention to details of critical care management, including mechanical ventilator settings, the procedure is safe even in patients with severe disease. However, further work is needed to define which patients, if any, experience a beneficial effect on outcome from this procedure. More research is needed on assessing efficacy of potential therapies within histologically defined subgroups. In the future, various biomarkers may be available to non-invasively classify ARDS patients from the standpoint of responsiveness to various therapies, such as glucocorticoids.

In this issue of *Critical Care*, Kao and colleagues [1] consider whether open lung biopsy (OLBx) can assist in the management of patients with acute respiratory distress syndrome (ARDS). Clinical outcome in ARDS remains poor despite substantial advances in our understanding of the biology of this syndrome [2]. Although limiting transpulmonary pressure can clearly prevent worsening of ARDS, no other major therapeutic advances with proven benefit have occurred in this area [3]. Progress has been limited potentially due to the heterogeneous phenotypes that are known to underlie the American European Consensus definition of this disease. Thus, methods to improve diagnostic specificity are likely to be helpful in making progress.

OLBx has been used for years as a method of defining the underlying pathology in patients with lung disease. While its role has become established in the setting of interstitial lung disease [4], its utility and safety are more controversial in critically ill patients. Proponents of OLBx argue that knowledge of underlying etiology can be helpful in defining the best course of treatment [5]. In addition, the risk of biopsy in experienced hands is fairly low if adequate precautions are taken [6]. Opponents of OLBx cite the lack of specific therapies for underlying etiologies of ARDS and believe that defining the underlying mechanism of injury is largely academic. A similar discussion has taken place in the interstitial lung disease arena, where some advocate the demonstration of usual interstitial pneumonitis among patients with idiopathic pulmonary fibrosis, whereas others believe that a therapeutic trial of steroids in the majority of patients is justifiable until new therapeutic strategies emerge [4,7].

The work by Kao and colleagues [1] supports the existing literature that open lung biopsy is fairly safe and frequently revealing in the context of ARDS. There are several take home points from this study. First, the authors corroborate prior reports that the underlying pathology in clinical ARDS is often a pattern other than diffuse alveolar damage or fibroproliferation. Of note, this and prior studies were retrospective analyses making the generalizability of these findings difficult to define. Without knowing the total number of ARDS cases potentially eligible for biopsy, we have no easy way to know how common the observed abnormalities would be in an unselected ARDS population.

Second, the authors found minimal morbidity attributable to the surgical procedures that their patients underwent. These data support the existing literature that, in experienced hands, OLBx can be safely performed in carefully chosen patients. The risk of bronchopleural fistula was fairly low in the present study, which may reflect the use of protective mechanical ventilation. We have recently observed that high pressures measured at the airway opening are strongly predictive of prolonged bronchopleural fistula risk following lung biopsy in ARDS [8]. Thus, attention to mechanical ventilator settings may be one factor that led to the low risk of this procedure.

ARDS = acute respiratory distress syndrome; OLBx = open lung biopsy.

Third, the authors report that results from OLBx did indeed affect clinical management. Nearly 75% of patients had changes made in their therapeutic management due to findings from OLBx. Whether these changes were helpful to the patient is not entirely clear due to the lack of a control group. However, at least 14 patients (11 with infections, 1 with hypersensitivity pneumonitis, and 2 with pulmonary edema) had a disorder found for which accepted therapies exist.

Interestingly, the most common change in management recorded in response to OLBx results was the institution of glucocorticoid therapy. The role of glucocorticoid therapy in ARDS has been controversial, with some smaller studies showing benefits whereas other larger studies demonstrated no important benefit [9,10]. A number of critiques have emerged after the recently published *New England Journal of Medicine* trial examining the role of steroids in persistent ARDS [10], leading some to speculate that, despite the negative results of that trial, some ARDS patients may still benefit from anti-inflammatory therapy. In this recent study, more than 95% of patients were excluded prior to enrollment, leading to results that may not be generalizable to the overall ARDS population. The most common reason for exclusion was glucocorticoid therapy, yielding the possibility that the best candidates for steroid therapy (from both an efficacy and safety perspective) were excluded from the study. In addition, the frequent use of paralytics (in up to 50% of steroid treated participants) and marked hyperglycemia (mean values in excess of 200 mg/dl) may have contributed to avoidable complications of steroid therapy. Thus, the frequent re-intubations and neuromyopathies that occurred in this recent study may have offset the potential benefits of steroid therapy. Regardless, the stratification of patients likely to benefit from steroid therapy, while avoiding the potential morbidity of pharmacological therapies and other intensive care unit measures (including mechanical ventilation) is likely to be a successful strategy. Future studies that aggressively limit the side effects of steroids and that examine treatment response stratified by OLBx findings may demonstrate subgroups of patients that derive important benefit from this therapy.

In the future, biomarkers that could be defined either in the serum or by bronchoalveolar lavage would be preferable to OLBx to stratify the likelihood of benefit from steroid therapy. Such biomarkers may help define the underlying pathobiology and so become a surrogate for OLBx in assessing the steroid responsiveness of the disease. Another class of biomarkers that may prove useful in the management of ARDS patients would be ones that provided information on the intrinsic steroid responsiveness of the patient [11,12]. The search for genetic polymorphisms that predict individual responsiveness to steroid therapies is well underway in other conditions such as asthma and ulcerative colitis. Both types of biomarkers would aid treatment decisions by better defining subgroups most likely to benefit from steroid therapy. Thus, further work is clearly needed to determine whether individualized therapy will improve outcome in various subgroups of ARDS patients.

Competing interests

The authors declare that they have no competing interests.

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